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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,394	05/16/2001	Naoto Miwa	SCH 1799	2377

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EXAMINER

SHARAREH, SHAHNAM J

ART UNIT PAPER NUMBER

1617

DATE MAILED: 08/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/787,394

Applicant(s)

MIWA ET AL.

Examiner

Shahnam Sharareh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 22 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 29,31,32 and 35-48 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 29,31,32 and 35-48 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 4/12/04.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission filed on April 12, 2004 has been entered.

Claims 29, 31-32, 35-48 are pending.

***Priority***

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Japan on September 1998. It is noted, however, that applicant has not filed a certified copy of the Japanese application as required by 35 U.S.C. 119(b).

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 41-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of claims 41-43 is directed to specific molecules having three sulfonic acid group which render the claims ambiguous, because their respective base claims can have sulfonic groups at various possible locations such as L<sub>1</sub>-L<sub>7</sub>, R<sub>19</sub>, R<sub>20</sub>, or R<sub>21</sub>-R<sub>28</sub> without adequately describing which positions

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can simultaneously have three different sulfonic groups in the molecule. Further, the specification fails to provide adequate descriptions of molecules having three different sulfonic groups and their respective positions in the molecule.

Accordingly, the metes and bounds of such claims are ambiguous.

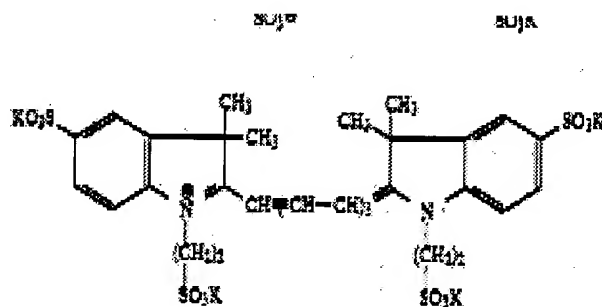
### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 29, 31-32, 35, 39-45 are rejected under 35 U.S.C. 102(b) as being anticipated by Ohno et al US Patent 4,839,265.
5. Ohno discloses water-soluble cyanine dyes comprising all features of the generic claim 1. Ohno at col 5-6 discloses the following compound, which is within the scope of the instant claims.



6. Specifically, this compound contain L<sub>1</sub>-L<sub>7</sub> as the CH=(CH-CH)<sub>3</sub> bridge. In this compound, L<sub>4</sub> would be an alkyl having 1 carbon atom. R<sup>21</sup> and R<sup>28</sup> are

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hydrogen atom or a sulfonic acid group. The R<sup>19</sup> and R<sup>20</sup> are lower alkyl group substituted by a sulfonic acid group. (also see col 5-6, examples 7; and col 7-8, example 13).

7. Ohno discloses at col 3, lines 20-25 that alkali metal salts include sodium salts:

molecule to have 4 to 6 sulfonic groups. In this specification, the sulfonic group represents a sulfo group and a salt thereof, and the carboxylic group represents a carboxyl group and a salt thereof. Examples of the salt include alkali metal salts (e.g., Na and K), ammonium salts, and organic ammonium salts (e.g., triethylamine,

Thus, Ohno discloses Na salts of his formula described above. Further, Ohno at col 13, lines 4-7 discloses dissolving his compounds in water or ethanol and mixing it in methyl cellulose. Water, ethanol and methyl cellulose are pharmaceutically acceptable excipients. Therefore, Ohno anticipates all limitations of the instant claims.

8. Applicant argues that Ohno does not disclose sodium salts instantly claimed. (see Remarks at page 9, 2<sup>nd</sup> – 3<sup>rd</sup> para.). In response, Examiner replies that contrary to Applicant's statement and as exhibited above in para. 2-3, Ohno's compositions meet the limitations of the instant claims.

9. At page 10, 3<sup>rd</sup> para., Applicant has argued that the compounds disclosed in Ohno have different degree of sulfonation and comparative data at page 84 of the specification has shown unexpected results and significant superiority in LD50 values of sodium salts when compared to potassium salts. In response,

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Examiner states that first of all the unexpected results do not impact anticipatory type rejections where all elements of the claims are disclosed in the prior art.

~~10~~. Second, the instant claims are not limited to any degree of sulfonation to exclude those described in Ohno. Therefore, Applicant's arguments are not commensurate with the scope of the rejected claims.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claims 29, 31-32, 35-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ohno et al US Patent 4,839,265 in view Licha et al US Patent 6,258,340 (Licha I) and further in view of Licha et al US Patent 6,083,485 (Licha II) and Randall US Patent 6,114,350.

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The teachings of Ohno are described above. Ohno teaches cyanine dyes see col 5-6, example 7. Ohno does not ~~teach~~ explicitly teach in vivo diagnostic use of his compounds.

12. Licha I discloses cyanine dye compositions for diagnostic use comprising same elements as the subgenus of the claim 29 (formula III-I). Specifically, Licha's formula (II a) wherein r is 1, L1 to L7 is CH, CR and R is alkyl or, R11 or R12 are alkyls, X or Y is C(CH<sub>3</sub>)<sub>2</sub>, Ch=CH or CR<sub>13</sub>R<sub>14</sub> wherein R<sub>13</sub>, R<sub>14</sub> are group W and W is either sulfonic acid or the formula III wherein Z is sulfoalkyls containing 2 to 4 atoms. (see col 17, lines 55-67, col 18, lines 1-64). Licha et al further disclose methods of using indole compounds for in vivo diagnostic procedures of identifying tumors, internal blood flow and angiography by administering to a patient indole compounds as set forth in his claim 1-4 (col 1, line 53-col 2, line 20; col 10, lines 30-67; col 13, lines 44-50; col 17, line 55-65; col 18, lines 30-65). The indole compounds of Licha meet all the instant subgenus as set forth in the instant claim 29, because Licha's compounds, as shown in col 17-18, comprise all the same substituents as instantly claimed. Therefore, cyanine groups within the subgenus of instant claim 29 have been shown to be effective for in vivo imaging.

13. Licha II and Randall are additional evidence essentially used to show the state of art at the time of invention with regards to the use of cyanine dyes in vivo.

Licha II teach the in vivo diagnostic use of various cyanine dyes that fall within the same scope as the instantly claimed compounds.

Randall discloses methods of diagnostic process using cyanine dyes that anticipates the limitations of the instant claims as set forth above (abstract; col 5, lines 14-40; col 6, lines 6-55; col 8, lines 14-22; table 1, compounds 18-28, specially compounds 24-26). The compounds disclosed by Randall comprise the same substituents as the subgenus set forth above and further contain sulfonic acid groups. Thus, Randall teaches cyanine derivatives that overlap in scope as the instant compounds that are used for diagnostic purposes.

14. Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to use the compounds of Ohno for diagnostic purposes, because as by Licha I, cyanine dyes within the subgenus group of compounds instantly claimed are used for in vivo diagnosis of tumors and assessments of blood flow.

The ordinary skill in the art would have had a reasonable expectation of observing diagnostic utility when using cyanine dyes of Ohno because as suggested by Licha I, the subgenus encompassing the instant compounds are successfully employed in the art for in vivo diagnostic methodologies. Further as provided by Licha II and Randall of cyanine dyes have been long for diagnostic use.

### ***Conclusion***

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.




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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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